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FULL ESTIMATED COST	0.15	0.15

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=> s "oil in water" and submicron and emulsion

L1 142 "OIL IN WATER" AND SUBMICRON AND EMULSION

=> dup rem l1

PROCESSING COMPLETED FOR L1
L2 76 DUP REM L1 (66 DUPLICATES REMOVED)

=> s l2 and adjuvant

L3 5 L2 AND ADJUVANT

=> d 1-5 bib ab

L3 ANSWER 1 OF 5 MEDLINE
AN 96376087 MEDLINE
DN 96376087
TI MF59 **adjuvant** enhances the immunogenicity of influenza vaccine in both young and old mice.
AU Higgins D A; Carlson J R; Van Nest G
CS Chiron Corporation, Emeryville, CA 94608, USA.
SO VACCINE, (1996 Apr) 14 (6) 478-84.
Journal code: X6O. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
AB The responses of young (8 week) and old (18 month) mice to influenza vaccine with and without the potent **emulsion adjuvant** MF59 were compared. In influenza naive mice, vaccine-specific antibody and T-cell proliferation were significantly lower in the old group compared to the young group. Post-immunization cytokine levels and antibody isotype profiles were different in the old compared to the young mice. The addition of the **adjuvant** MF59, a **submicron oil** -in-**water emulsion** composed of 5% v/v squalene, 0.5% v/v Tween 80 and 0.5% v/v Span 85, significantly increased the immune responses of both the young and old naive mice to the vaccine. The responses of the old mice given **adjuvant** increased to levels equivalent to those of young mice with vaccine alone. In mice previously infected with influenza virus, similarly depressed immune responses to vaccination were detected in the old mice. While the addition of MF59 to the vaccine had little effect on antibody titres of the previously infected young mice, the **adjuvant** significantly increased the antibody responses of the previously infected old mice. These results suggest that influenza vaccine combined with MF59 may significantly improve immune responses of elderly humans to influenza vaccination.

L3 ANSWER 2 OF 5 MEDLINE
AN 96164471 MEDLINE
DN 96164471
TI Enhancement of humoral response against human influenza vaccine with the simple **submicron oil/water emulsion adjuvant** MF59.
AU Ott G; Barchfeld G L; Van Nest G
CS Chiron Corporation, Emeryville, CA 94608, USA.
SO VACCINE, (1995 Nov) 13 (16) 1557-62.
Journal code: X6O. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199605
AB Human influenza subunit vaccines are not fully protective in either the very young or elderly populations where risk is greatest. The use of an **adjuvant** to enhance antibody titer is an attractive option to increase vaccine efficacy. A series of squalene/H2O emulsions stabilized either by the amphipathic muramyl peptide MTP-PE (sodium N-acetyl-muramyl-L-alanyl-D-isoglutaminyl-L-alanyl-2-(1',2'-dipalmitoyl-sn- glycero-3'phospho) ethylamide) or by mixtures of the sorbitan oleate surfactants Tween 80 and Span 85 have been tested as adjuvants with influenza vaccine. Combination of influenza vaccine with the Tween/Span stabilized emulsions has resulted in significantly higher antibody titers to vaccine in an extensive series of naive animal models. The use of **submicron emulsion** droplets is significant in determination of **adjuvant** activity while the presence of the muramyl peptide is not required for **adjuvant** activity. The 200-300 nm diameter **emulsion** formulation MF59 containing only the low toxicity components squalene, Tween 80 and Span 85 has been shown to enhance titers from 5 to 250 times that achievable with vaccine alone.

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS
AN 1999:70411 CAPLUS
DN 130:129990
TI Use of **submicron oil**-in-**water** emulsions with DNA vaccines
IN McCormak, James E.; Jolly, Douglas J.; Van, Nest Gary
PA Chiron Corporation, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9902132	A2	19990121	WO 1998-US14310	19980708
	WO 9902132	A3	19990812		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9882982	A1	19990208	AU 1998-82982	19980708
PRAI	US 1997-51944	19970708			
	US 1997-54756	19970805			
	WO 1998-US14310	19980708			

AB The use of **submicron oil**-in-**water** emulsions

with nucleic acid immunization techniques is disclosed. The method includes immunization with vaccine compns. contg. nucleic acid mols. encoding one or more antigens of interest, as well as administration of a **submicron oil-in-water adjuvant**, such as MF59. The **adjuvant** can be administered either before, after or simultaneously with the nucleic acid vaccines.

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2000 ACS
AN 1995:698952 CAPLUS
DN 123:93246
TI **Submicron** emulsions as vaccine adjuvants
IN Lowell, George H.; Amselem, Shimon; Friedman, Doron; Aviv, Haim
PA Pharmos Corp., USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9511700	A1	19950504	WO 1993-US10402	19931029
W: AT, AU, BB, BG, BR, BY, CA, CZ, DE, DK, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9455432	A1	19950522	AU 1994-55432	19931029
US 5961970	A	19991005	US 1996-637756	19960429
US 5985284	A	19991116	US 1996-677302	19960709
PRAI WO 1993-US10402	19931029			
US 1996-637756	19960429			

AB A vaccine **adjuvant** comprises an **oil-in-water submicron emulsion** that has 0.5-50% of an oil, 0.1-10% of an emulsifier, 0.5-5% of a nonionic surfactant, 0.00001-1% of an immunogen, and an aq. continuous phase. This **submicron emulsion** has a mean droplet size in the range of 0.03-0.5 .mu.m, and preferably 0.05-0.2 .mu.m.

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2000 ACS
AN 1991:542253 CAPLUS
DN 115:142253
TI **Adjuvant** formulation comprising a **submicron** oil droplet **emulsion**
IN Van Nest, Gary; Ott, Gary; Barchfeld, Gail
PA Chiron Corp., USA
SO Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 399843	A2	19901128	EP 1990-305744	19900525
EP 399843	A3	19920902		
EP 399843	B1	19940713		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2017507	AA	19901125	CA 1990-2017507	19900524
CA 2017507	C	19961112		
WO 9014837	A1	19901213	WO 1990-US2954	19900524
W: HU, JP				
HU 61203	A2	19921228	HU 1990-5459	19900524
HU 212924	B	19961230		
JP 05508385	T2	19931125	JP 1990-509214	19900524

JP 08032638 B4 19960329
DD 294633 A5 19911010 DD 1990-341001 19900525
ES 2033626 T3 19941016 ES 1990-305744 19900525
PRAI US 1989-357035 19890525
WO 1990-US2954 19900524
OS MARPAT 115:142253
AB An **adjuvant** compn. comprises a metabolizable oil and an emulsifying agent in an **oil**-in-**water emulsion** having oil droplets <1 .mu.m in diam. Preferably, the emulsifying agent is also an immunostimulating agent, e.g. a lipophilic muramyl peptide. Alternatively, an immunostimulating agent sep. from the emulsifying agent can be used. Goats were immunized with herpes simplex virus gD2 antigen (recombinant glycosylated protein with truncated anchor region) in squalene 4% and MTP-PE (N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-[1,2-dipalmitoyl-sn-glycero-3-(hydroxyphosphoryloxy)]ethylamide) 500 .mu.g/mL. The oil droplets in the **emulsion** were 0.5-0.6 .mu.m. This formulation gave the highest antibody titers.

=> log h

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	18.13	18.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.67	-1.67

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